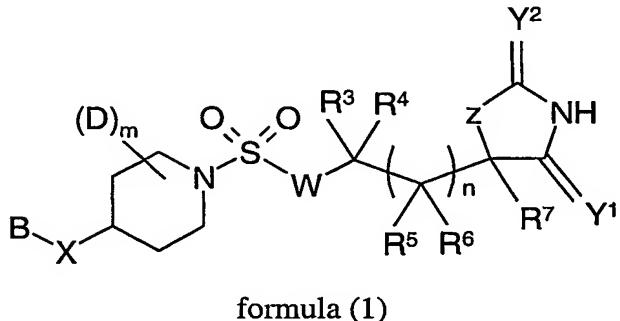


**CLAIMS**

We claim:

1. A compound of formula (1) or a pharmaceutically acceptable salt thereof:



5

wherein:

**Y<sup>1</sup>** and **Y<sup>2</sup>** are independently O or S;

**z** is NR<sup>8</sup>, O or S;

10 **n** is 0 or 1;

**W** is NR<sup>1</sup>, CR<sup>1</sup>R<sup>2</sup> or a bond;

**m** is 0 or 1;

**D** is hydrogen, C<sub>1-4</sub>alkyl, C<sub>3-6</sub>cycloalkyl or fluoro;

**X** is -(CR<sup>12</sup>R<sup>13</sup>)<sub>t</sub>-Q-(CR<sup>14</sup>R<sup>15</sup>)<sub>u</sub>- where t and u are independently 0 or 1 and Q is O, S, SO or

15 SO<sub>2</sub>;

**B** is a group selected from aryl, heteroaryl and heterocyclyl, where each group is optionally substituted by one or more groups independently selected from nitro, trifluoromethyl, trifluoromethoxy, halo, cyano, C<sub>1-4</sub>alkyl (optionally substituted by R<sup>9</sup> or C<sub>1-4</sub>alkoxy or one or more halo), C<sub>2-4</sub>alkenyl (optionally substituted by halo or R<sup>9</sup>), C<sub>2-4</sub>alkynyl (optionally substituted by halo or R<sup>9</sup>), C<sub>3-6</sub>cycloalkyl (optionally substituted by R<sup>9</sup> or one or more halo), C<sub>5-6</sub>cycloalkenyl (optionally substituted by halo or R<sup>9</sup>), aryl (optionally substituted by halo or C<sub>1-4</sub>alkyl), heteroaryl (optionally substituted by halo or C<sub>1-4</sub>alkyl), heterocyclyl (optionally substituted by C<sub>1-4</sub>alkyl), -SR<sup>11</sup>, -SOR<sup>11</sup>, -SO<sub>2</sub>R<sup>11</sup>, -SO<sub>2</sub>NR<sup>9</sup>R<sup>10</sup>, -NR<sup>9</sup>SO<sub>2</sub>R<sup>11</sup>, -NHCONR<sup>9</sup>R<sup>10</sup>, -OR<sup>9</sup>, -NR<sup>9</sup>R<sup>10</sup>, -CONR<sup>9</sup>R<sup>10</sup> and -NR<sup>9</sup>COR<sup>10</sup>; or B is C<sub>2-4</sub>alkenyl or C<sub>2-4</sub>alkynyl, each being optionally substituted by a group selected from C<sub>1-4</sub>alkyl, C<sub>3-6</sub>cycloalkyl, aryl, heteroaryl and heterocyclyl which group is optionally substituted by one or more halo,

nitro, cyano, trifluoromethyl, trifluoromethoxy,  $-\text{CONHR}^9$ ,  $-\text{CONR}^9\text{R}^{10}$ ,  $-\text{SO}_2\text{R}^{11}$ ,  $-\text{SO}_2\text{NR}^9\text{R}^{10}$ ,  $-\text{NR}^9\text{SO}_2\text{R}^{11}$ ,  $\text{C}_{1-4}\text{alkyl}$  or  $\text{C}_{1-4}\text{alkoxy}$ ; with the provisos that:

when n is 1 and W is  $\text{NR}^1$ ,  $\text{CR}^1\text{R}^2$  or a bond; or when n is 0 and W is  $\text{CR}^1\text{R}^2$ ; then B is a group selected from aryl, heteroaryl and heterocyclyl, where each group is optionally

- 5 substituted by one or more groups independently selected from nitro, trifluoromethyl, trifluoromethoxy, halo, cyano,  $\text{C}_{1-4}\text{alkyl}$  (optionally substituted by  $\text{R}^9$  or  $\text{C}_{1-4}\text{alkoxy}$  or one or more halo),  $\text{C}_{2-4}\text{alkenyl}$  (optionally substituted by halo or  $\text{R}^9$ ),  $\text{C}_{2-4}\text{alkynyl}$  (optionally substituted by halo or  $\text{R}^9$ ),  $\text{C}_{3-6}\text{cycloalkyl}$  (optionally substituted by  $\text{R}^9$  or one or more halo),  $\text{C}_{5-6}\text{cycloalkenyl}$  (optionally substituted by halo or  $\text{R}^9$ ), aryl (optionally substituted by halo or  $\text{C}_{1-4}\text{alkyl}$ ), heteroaryl (optionally substituted by halo or  $\text{C}_{1-4}\text{alkyl}$ ), heterocyclyl (optionally substituted by  $\text{C}_{1-4}\text{alkyl}$ ),  $-\text{SR}^{11}$ ,  $-\text{SOR}^{11}$ ,  $-\text{SO}_2\text{R}^{11}$ ,  $-\text{SO}_2\text{NR}^9\text{R}^{10}$ ,  $-\text{NR}^9\text{SO}_2\text{R}^{11}$ ,  $-\text{NHCONR}^9\text{R}^{10}$ ,  $-\text{OR}^9$ ,  $-\text{NR}^9\text{R}^{10}$ ,  $-\text{CONR}^9\text{R}^{10}$  and  $-\text{NR}^9\text{COR}^{10}$ ; or B is  $\text{C}_{2-4}\text{alkenyl}$  or  $\text{C}_{2-4}\text{alkynyl}$ , each being optionally substituted by a group selected from  $\text{C}_{1-4}\text{alkyl}$ ,  $\text{C}_{3-6}\text{cycloalkyl}$ , aryl, heteroaryl and heterocyclyl which group is optionally substituted by one or more halo,
- 10 nitro, cyano, trifluoromethyl, trifluoromethoxy,  $-\text{CONHR}^9$ ,  $-\text{CONR}^9\text{R}^{10}$ ,  $-\text{SO}_2\text{R}^{11}$ ,  $-\text{SO}_2\text{NR}^9\text{R}^{10}$ ,  $-\text{NR}^9\text{SO}_2\text{R}^{11}$ ,  $\text{C}_{1-4}\text{alkyl}$  or  $\text{C}_{1-4}\text{alkoxy}$ ; and
- 15 when n is 0 and W is  $\text{NR}^1$  or a bond; then B is a group selected from bicyclic aryl, bicyclic heteroaryl and bicyclic heterocyclyl, where each group is optionally substituted by one or more groups independently selected from nitro, trifluoromethyl, trifluoromethoxy, halo,
- 20 cyano,  $\text{C}_{1-4}\text{alkyl}$  (optionally substituted by  $\text{R}^9$  or  $\text{C}_{1-4}\text{alkoxy}$  or one or more halo),  $\text{C}_{2-4}\text{alkenyl}$  (optionally substituted by halo or  $\text{R}^9$ ),  $\text{C}_{2-4}\text{alkynyl}$  (optionally substituted by halo or  $\text{R}^9$ ),  $\text{C}_{3-6}\text{cycloalkyl}$  (optionally substituted by  $\text{R}^9$  or one or more halo),  $\text{C}_{5-6}\text{cycloalkenyl}$  (optionally substituted by halo or  $\text{R}^9$ ), aryl (optionally substituted by halo or  $\text{C}_{1-4}\text{alkyl}$ ), heteroaryl (optionally substituted by halo or  $\text{C}_{1-4}\text{alkyl}$ ), heterocyclyl (optionally substituted by  $\text{C}_{1-4}\text{alkyl}$ ),
- 25  $-\text{SR}^{11}$ ,  $-\text{SOR}^{11}$ ,  $-\text{SO}_2\text{R}^{11}$ ,  $-\text{SO}_2\text{NR}^9\text{R}^{10}$ ,  $-\text{NR}^9\text{SO}_2\text{R}^{11}$ ,  $-\text{NHCONR}^9\text{R}^{10}$ ,  $-\text{OR}^9$ ,  $-\text{NR}^9\text{R}^{10}$ ,  $-\text{CONR}^9\text{R}^{10}$  and  $-\text{NR}^9\text{COR}^{10}$ ; or B is  $\text{C}_{2-4}\text{alkenyl}$  or  $\text{C}_{2-4}\text{alkynyl}$ , each being optionally substituted by a group selected from  $\text{C}_{1-4}\text{alkyl}$ ,  $\text{C}_{3-6}\text{cycloalkyl}$ , aryl, heteroaryl and heterocyclyl which group is optionally substituted by one or more halo, nitro, cyano, trifluoromethyl, trifluoromethoxy,  $-\text{CONHR}^9$ ,  $-\text{CONR}^9\text{R}^{10}$ ,  $-\text{SO}_2\text{R}^{11}$ ,  $-\text{SO}_2\text{NR}^9\text{R}^{10}$ ,  $-\text{NR}^9\text{SO}_2\text{R}^{11}$ ,  $\text{C}_{1-4}\text{alkyl}$  or
- 30  $\text{C}_{1-4}\text{alkoxy}$ ;

**R<sup>1</sup>** and **R<sup>2</sup>** are independently hydrogen or a group selected from C<sub>1-6</sub>alkyl, C<sub>2-6</sub>alkenyl, C<sub>2-6</sub>alkynyl, C<sub>3-6</sub>cycloalkyl and C<sub>5-6</sub>cycloalkenyl which group may be optionally substituted by halo, cyano, hydroxy or C<sub>1-4</sub>alkoxy;

- R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup> and R<sup>6</sup>** are independently hydrogen or a group selected from C<sub>1-6</sub>alkyl, C<sub>2-6</sub>alkenyl, C<sub>2-6</sub>alkynyl, C<sub>3-6</sub>cycloalkyl, C<sub>5-6</sub>cycloalkenyl, aryl, heteroaryl and heterocyclyl which group is optionally substituted by one or more substituents independently selected from halo, nitro, cyano, trifluoromethyl, trifluoromethoxy, C<sub>1-4</sub>alkyl, C<sub>2-4</sub>alkenyl, C<sub>2-4</sub>alkynyl, C<sub>3-6</sub>cycloalkyl (optionally substituted by one or more R<sup>17</sup>), aryl (optionally substituted by one or more R<sup>17</sup>), heteroaryl (optionally substituted by one or more R<sup>17</sup>), heterocyclyl, -OR<sup>18</sup>, -SR<sup>19</sup>, -SOR<sup>19</sup>, -SO<sub>2</sub>R<sup>19</sup>, -COR<sup>19</sup>, -CO<sub>2</sub>R<sup>18</sup>, -CONR<sup>18</sup>R<sup>20</sup>, -NR<sup>16</sup>COR<sup>18</sup>, -SO<sub>2</sub>NR<sup>18</sup>R<sup>20</sup> and -NR<sup>16</sup>SO<sub>2</sub>R<sup>19</sup>; or **R<sup>1</sup>** and **R<sup>3</sup>** together with the nitrogen or carbon atoms and carbon atom to which they are respectively attached form a saturated 3- to 7-membered ring optionally containing 1 or 2 heteroatom groups selected from NH, O, S, SO and SO<sub>2</sub> where the ring is optionally substituted on carbon by C<sub>1-4</sub>alkyl, fluoro or C<sub>1-4</sub>alkoxy and/or on nitrogen by -COC<sub>1-3</sub>alkyl, -SO<sub>2</sub>C<sub>1-3</sub>alkyl or C<sub>1-4</sub>alkyl; or **R<sup>3</sup>** and **R<sup>4</sup>** together form a saturated 3- to 7-membered ring optionally containing 1 or 2 heteroatom groups selected from NH, O, S, SO and SO<sub>2</sub> where the ring is optionally substituted on carbon by C<sub>1-4</sub>alkyl, fluoro or C<sub>1-4</sub>alkoxy and/or on nitrogen by -COC<sub>1-3</sub>alkyl, -SO<sub>2</sub>C<sub>1-3</sub>alkyl or C<sub>1-4</sub>alkyl; or **R<sup>5</sup>** and **R<sup>6</sup>** together form a saturated 3- to 7-membered ring optionally containing 1 or 2 heteroatom groups selected from NH, O, S, SO and SO<sub>2</sub> where the ring is optionally substituted on carbon by C<sub>1-4</sub>alkyl, fluoro or C<sub>1-4</sub>alkoxy and/or on nitrogen by -COC<sub>1-3</sub>alkyl, -SO<sub>2</sub>C<sub>1-3</sub>alkyl or C<sub>1-4</sub>alkyl;
- R<sup>7</sup>** is hydrogen or a group selected from C<sub>1-6</sub>alkyl, C<sub>2-6</sub>alkenyl, C<sub>2-6</sub>alkynyl, heteroalkyl, C<sub>3-7</sub>cycloalkyl, aryl, heteroaryl or heterocyclyl where the group is optionally substituted by halo, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkoxy, C<sub>3-7</sub>cycloalkyl, heterocyclyl, aryl, heteroaryl or heteroalkyl; and wherein the group from which **R<sup>7</sup>** may be selected is optionally substituted on the group and/or on its optional substituent by one or more substituents independently selected from halo, cyano, C<sub>1-4</sub>alkyl, nitro, haloC<sub>1-4</sub>alkyl, heteroalkyl, aryl, heteroaryl, hydroxyC<sub>1-4</sub>alkyl, C<sub>3-7</sub>cycloalkyl, heterocyclyl, C<sub>1-4</sub>alkoxyC<sub>1-4</sub>alkyl, haloC<sub>1-4</sub>alkoxyC<sub>1-4</sub>alkyl, -COC<sub>1-4</sub>alkyl, -OR<sup>21</sup>, -CO<sub>2</sub>R<sup>21</sup>, -SOR<sup>25</sup>, -SO<sub>2</sub>R<sup>25</sup>, -NR<sup>21</sup>COR<sup>22</sup>, -CONR<sup>21</sup>R<sup>22</sup> and -NHCONR<sup>21</sup>R<sup>22</sup>;

or  $\mathbf{R}^3$  and  $\mathbf{R}^7$  together with the carbon atoms to which they are each attached and  $(\mathbf{CR}^5\mathbf{R}^6)_n$  form a saturated 5- to 7-membered ring optionally containing a heteroatom group selected from NH, O, S, SO and SO<sub>2</sub> where the ring is optionally substituted on carbon by C<sub>1-4</sub>alkyl, fluoro or C<sub>1-4</sub>alkoxy and/or on nitrogen by -COC<sub>1-3</sub>alkyl, -SO<sub>2</sub>C<sub>1-3</sub>alkyl or C<sub>1-4</sub>alkyl;

5     $\mathbf{R}^8$  is selected from hydrogen, C<sub>1-6</sub>alkyl and haloC<sub>1-6</sub>alkyl;

$\mathbf{R}^9$  and  $\mathbf{R}^{10}$  are independently hydrogen, C<sub>1-6</sub>alkyl or C<sub>3-6</sub>cycloalkyl;

or  $\mathbf{R}^9$  and  $\mathbf{R}^{10}$  together with the nitrogen to which they are attached form a heterocyclic 4 to 7-membered ring.

$\mathbf{R}^{11}$  is C<sub>1-6</sub>alkyl or C<sub>3-6</sub>cycloalkyl;

10    $\mathbf{R}^{12}$ ,  $\mathbf{R}^{13}$ ,  $\mathbf{R}^{14}$  and  $\mathbf{R}^{15}$  are independently selected from hydrogen, C<sub>1-6</sub>alkyl and C<sub>3-6</sub>cycloalkyl;

$\mathbf{R}^{16}$  is hydrogen or C<sub>1-6</sub>alkyl;

$\mathbf{R}^{17}$  is selected from halo, C<sub>1-6</sub>alkyl, C<sub>3-6</sub>cycloalkyl and C<sub>1-6</sub>alkoxy;

$\mathbf{R}^{18}$  is hydrogen or a group selected from C<sub>1-6</sub>alkyl, C<sub>3-6</sub>cycloalkyl, C<sub>5-7</sub>cycloalkenyl, saturated heterocyclyl, aryl, heteroaryl, arylC<sub>1-4</sub>alkyl and heteroarylC<sub>1-4</sub>alkyl which group is optionally

15   substituted by one or more halo;

$\mathbf{R}^{19}$  and  $\mathbf{R}^{25}$  are independently a group selected from C<sub>1-6</sub>alkyl, C<sub>3-6</sub>cycloalkyl, C<sub>5-7</sub>cycloalkenyl, saturated heterocyclyl, aryl, heteroaryl, arylC<sub>1-4</sub>alkyl and heteroarylC<sub>1-4</sub>alkyl

which group is optionally substituted by one or more halo;

$\mathbf{R}^{20}$  is hydrogen, C<sub>1-6</sub>alkyl or C<sub>3-6</sub>cycloalkyl;

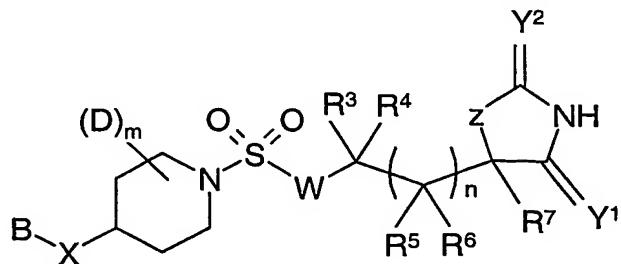
20   or  $\mathbf{R}^{18}$  and  $\mathbf{R}^{20}$  together with the nitrogen to which they are attached form a heterocyclic 4- to 7-membered ring;

$\mathbf{R}^{21}$  and  $\mathbf{R}^{22}$  are independently hydrogen, C<sub>1-4</sub>alkyl, haloC<sub>1-4</sub>alkyl, aryl and arylC<sub>1-4</sub>alkyl;

or  $\mathbf{R}^{21}$  and  $\mathbf{R}^{22}$  together with the nitrogen to which they are attached form a heterocyclic 5- to 6-membered ring.

25

2.      A compound of formula (1) or a pharmaceutically acceptable salt thereof:



wherein:

**Y<sup>1</sup>** and **Y<sup>2</sup>** are independently O or S;

**z** is NR<sup>8</sup>, O or S;

**n** is 0;

5 **W** is NR<sup>1</sup>;

**m** is 0 or 1;

**D** is hydrogen, C<sub>1-4</sub>alkyl, C<sub>3-6</sub>cycloalkyl or fluoro;

**X** is -(CR<sup>12</sup>R<sup>13</sup>)<sub>t</sub>-Q-(CR<sup>14</sup>R<sup>15</sup>)<sub>u</sub>- where t and u are independently 0 or 1 and Q is O, S, SO or SO<sub>2</sub>;

10 **B** is a group selected from aryl, heteroaryl and heterocyclyl, where each group is optionally substituted by one or more groups independently selected from nitro, trifluoromethyl, trifluoromethoxy, halo, cyano, C<sub>1-4</sub>alkyl (optionally substituted by R<sup>9</sup> or C<sub>1-4</sub>alkoxy or one or more halo), C<sub>2-4</sub>alkenyl (optionally substituted by halo or R<sup>9</sup>), C<sub>2-4</sub>alkynyl (optionally substituted by halo or R<sup>9</sup>), C<sub>3-6</sub>cycloalkyl (optionally substituted by R<sup>9</sup> or one or more halo),

15 C<sub>5-6</sub>cycloalkenyl (optionally substituted by halo or R<sup>9</sup>), aryl (optionally substituted by halo or C<sub>1-4</sub>alkyl), heteroaryl (optionally substituted by halo or C<sub>1-4</sub>alkyl), heterocyclyl (optionally substituted by C<sub>1-4</sub>alkyl), -SR<sup>11</sup>, -SOR<sup>11</sup>, -SO<sub>2</sub>R<sup>11</sup>, -SO<sub>2</sub>NR<sup>9</sup>R<sup>10</sup>, -NR<sup>9</sup>SO<sub>2</sub>R<sup>11</sup>, -NHCONR<sup>9</sup>R<sup>10</sup>, -OR<sup>9</sup>, -CONR<sup>9</sup>R<sup>10</sup> and -NR<sup>9</sup>COR<sup>10</sup>;

**R<sup>1</sup>** is hydrogen or a group selected from C<sub>1-6</sub>alkyl, C<sub>2-6</sub>alkenyl, C<sub>2-6</sub>alkynyl, C<sub>3-6</sub>cycloalkyl and

20 C<sub>5-6</sub>cycloalkenyl which group may be optionally substituted by halo, cyano, hydroxy or C<sub>1-4</sub>alkoxy;

**R<sup>3</sup>** and **R<sup>4</sup>** are independently hydrogen or a group selected from C<sub>1-4</sub>alkyl, C<sub>2-4</sub>alkenyl, C<sub>2-4</sub>alkynyl, C<sub>3-5</sub>cycloalkyl, pentenyl, aryl, heteroaryl and heterocyclyl which group is optionally substituted by one or more substituents independently selected from halo, nitro, cyano,

25 trifluoromethyl, trifluoromethoxy, C<sub>1-4</sub>alkyl, C<sub>2-4</sub>alkenyl, C<sub>2-4</sub>alkynyl, C<sub>3-6</sub>cycloalkyl (optionally substituted by one or more R<sup>17</sup>), aryl (optionally substituted by one or more R<sup>17</sup>), heteroaryl (optionally substituted by one or more R<sup>17</sup>), heterocyclyl, -OR<sup>18</sup>, -SR<sup>19</sup>, -SOR<sup>19</sup>, -SO<sub>2</sub>R<sup>19</sup>, -CONR<sup>18</sup>R<sup>20</sup> and -NR<sup>16</sup>COR<sup>18</sup>,

or **R<sup>1</sup>** and **R<sup>3</sup>** together with the nitrogen and carbon atoms to which they are respectively

30 attached form a saturated 3- to 7-membered ring optionally containing 1 or 2 heteroatom groups selected from NH, O, S, SO and SO<sub>2</sub> where the ring is optionally substituted on carbon

- by C<sub>1-4</sub>alkyl, fluoro or C<sub>1-4</sub>alkoxy and/or on nitrogen by -COC<sub>1-3</sub>alkyl, -SO<sub>2</sub>C<sub>1-3</sub>alkyl or C<sub>1-4</sub>alkyl;
- or R<sup>3</sup> and R<sup>4</sup> together form a carbocyclic or saturated heterocyclic 3- to 7-membered ring optionally containing 1 or 2 heteroatom groups selected from NH, O, S, SO and SO<sub>2</sub> where
- 5 the ring is optionally substituted on carbon by C<sub>1-4</sub>alkyl, fluoro or C<sub>1-4</sub>alkoxy and/or on nitrogen by -COC<sub>1-3</sub>alkyl, -SO<sub>2</sub>C<sub>1-3</sub>alkyl or C<sub>1-4</sub>alkyl;
- R<sup>7</sup> is hydrogen or a group selected from C<sub>1-4</sub>alkyl, heteroalkyl, C<sub>3-5</sub>cycloalkyl, aryl, heteroaryl or heterocyclyl which group is optionally substituted by halo, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkoxy, C<sub>3-5</sub>cycloalkyl, heterocyclyl, aryl, heteroaryl or heteroalkyl; and wherein the group from which R<sup>7</sup>
- 10 may be selected is optionally substituted on the group and/or on its optional substituent by one or more substituents independently selected from halo, cyano, C<sub>1-4</sub>alkyl, nitro, haloC<sub>1-4</sub>alkyl, heteroalkyl, aryl, heteroaryl, hydroxyC<sub>1-4</sub>alkyl, C<sub>3-5</sub>cycloalkyl, heterocyclyl, C<sub>1-4</sub>alkoxyC<sub>1-4</sub>alkyl, haloC<sub>1-4</sub>alkoxyC<sub>1-4</sub>alkyl, -COC<sub>1-4</sub>alkyl, -OR<sup>21</sup>, -CO<sub>2</sub>R<sup>21</sup>, -SR<sup>25</sup>, -SOR<sup>25</sup>, -SO<sub>2</sub>R<sup>25</sup>, -CONR<sup>21</sup>R<sup>22</sup> and -NHCONR<sup>21</sup>R<sup>22</sup>;
- 15 or R<sup>3</sup> and R<sup>7</sup> together with the carbon atoms to which they are each attached and (CR<sup>5</sup>R<sup>6</sup>)<sub>n</sub> form a saturated carbocyclic or heterocyclic 5- or 6-membered ring;
- R<sup>8</sup> is selected from hydrogen, C<sub>1-4</sub>alkyl and haloC<sub>1-4</sub>alkyl;
- R<sup>9</sup> and R<sup>10</sup> are independently hydrogen, C<sub>1-6</sub>alkyl or C<sub>3-6</sub>cycloalkyl;
- or R<sup>9</sup> and R<sup>10</sup> together with the nitrogen to which they are attached form a heterocyclic 4 to 6-
- 20 membered ring.
- R<sup>11</sup> is C<sub>1-4</sub>alkyl or C<sub>3-5</sub>cycloalkyl;
- R<sup>12</sup>, R<sup>13</sup>, R<sup>14</sup> and R<sup>15</sup> are independently selected from hydrogen, C<sub>1-4</sub>alkyl and C<sub>3-4</sub>cycloalkyl;
- R<sup>16</sup> is hydrogen or C<sub>1-4</sub>alkyl;
- R<sup>17</sup> is selected from halo, C<sub>1-4</sub>alkyl, C<sub>3-5</sub>cycloalkyl and C<sub>1-4</sub>alkoxy;
- 25 R<sup>18</sup> is hydrogen or a group selected from C<sub>1-4</sub>alkyl, C<sub>3-5</sub>cycloalkyl, C<sub>5-6</sub>cycloalkenyl, saturated heterocyclyl, aryl, heteroaryl, arylC<sub>1-4</sub>alkyl and heteroarylC<sub>1-4</sub>alkyl which group is optionally substituted by one or more halo;
- R<sup>19</sup> and R<sup>25</sup> are independently a group selected from C<sub>1-4</sub>alkyl, C<sub>3-5</sub>cycloalkyl, C<sub>5-6</sub>cycloalkenyl, saturated heterocyclyl, aryl, heteroaryl, arylC<sub>1-4</sub>alkyl and heteroarylC<sub>1-4</sub>alkyl
- 30 which group is optionally substituted by one or more halo;
- R<sup>20</sup> is hydrogen, C<sub>1-4</sub>alkyl or C<sub>3-5</sub>cycloalkyl;

or  $\mathbf{R}^{18}$  and  $\mathbf{R}^{20}$  together with the nitrogen to which they are attached form a heterocyclic 4- to 6-membered ring;

$\mathbf{R}^{21}$  and  $\mathbf{R}^{22}$  are independently hydrogen,  $C_{1-4}$ alkyl, halo $C_{1-4}$ alkyl, aryl and aryl $C_{1-4}$ alkyl;

or  $\mathbf{R}^{21}$  and  $\mathbf{R}^{22}$  together with the nitrogen to which they are attached form a heterocyclic 5- to 6-membered ring.

3. A compound according to claim 1 wherein B is phenyl, naphthyl, pyridyl, quinolinyl, isoquinolinyl, thienopyridyl, naphthyridinyl, 2,3-methylenedioxyphenyl, 3,4-methylenedioxyphenyl, thienopyrimidinyl, pyridoimidazolyl, benzimidazolyl, benzofuranyl, 10 benzothienyl, indolyl, benzothiazolyl, benzotriazolyl, benzisoxazolyl, benzisothiazolyl, indazolyl, indolizinyl, isobenzofuranyl, quinazolinyl, imidazopyridinyl, pyrazolopyridinyl, indolinyl, tetrahydroquinolinyl, tetrahydroisoquinolinyl or isoindolinyl, where each is optionally substituted by one or more groups independently selected from nitro, trifluoromethyl, trifluoromethoxy, halo,  $C_{1-4}$ alkyl (optionally substituted by one or more halo), 15  $C_{2-4}$ alkynyl, heteroaryl,  $-OR^9$ , cyano,  $-NR^9R^{10}$ ,  $-CONR^9R^{10}$  and  $-NR^9COR^{10}$ ; or B is vinyl or ethynyl optionally substituted by  $C_{1-4}$ alkyl.

4. A compound according to claim 1 or 2 wherein B is a group selected from bicyclic aryl, bicyclic heteroaryl and bicyclic heterocyclyl, where each group is optionally substituted 20 by one or more groups independently selected from nitro, trifluoromethyl, trifluoromethoxy, halo,  $C_{1-4}$ alkyl (optionally substituted by one or more halo),  $C_{2-4}$ alkynyl, heteroaryl,  $-OR^9$ , cyano,  $-NR^9R^{10}$ ,  $-CONR^9R^{10}$  and  $-NR^9COR^{10}$ ; or B is  $C_{2-4}$ alkenyl or  $C_{2-4}$ alkynyl optionally substituted by  $C_{1-4}$ alkyl,  $C_{3-6}$ cycloalkyl or heterocyclyl.

25 5. A compound according to claim 1 or 2 wherein B is 2-methylquinolin-4-yl.

6. A compound according to any one of the preceding claims wherein  $R^7$  is hydrogen or a group selected from  $C_{1-4}$ alkyl, aryl $C_{1-4}$ alkyl, heteroaryl $C_{1-4}$ alkyl, heterocyclyl $C_{1-4}$ alkyl, aryl, heteroaryl, heterocyclyl and  $C_{3-5}$ cycloalkyl which group is optionally substituted by cyano,  $C_{1-4}$ alkyl, halo,  $-OR^{21}$ ,  $-NR^{21}R^{22}$ ,  $-CO_2R^{21}$  and  $-NR^{21}CO_2R^{22}$ .

7. A compound according to claim 6 wherein R<sup>7</sup> is hydrogen or C<sub>1-4</sub>alkyl optionally substituted with halo, hydroxy or C<sub>1-3</sub>alkoxy.

8. A pharmaceutical composition comprising a compound according to claim 1 or claim 5 2; and a pharmaceutically-acceptable diluent or carrier.

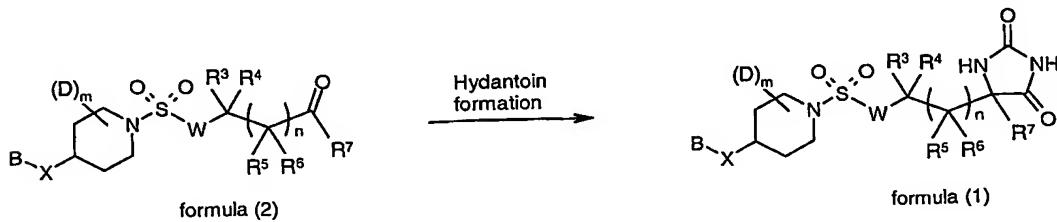
9. A compound according to claim 1 or 2 for use as a medicament.

10. The use of a compound according to claim 1 or 2 in the manufacture of a medicament 10 in the treatment of a disease condition mediated TNF- $\alpha$ .

11. The use of a compound according to claim 1 or 2 in the manufacture of a medicament in the treatment of autoimmune disease, allergic/atopic diseases, transplant rejection, graft versus host disease, cardiovascular disease, reperfusion injury and malignancy in a warm-blooded animal such as man.

12. A method of treating autoimmune disease, allergic/atopic diseases, transplant rejection, graft versus host disease, cardiovascular disease, reperfusion injury and malignancy in a warm-blooded animal, such as man, in need of such treatment which comprises 20 administering to said animal an effective amount of a compound according to claim 1 or 2.

13. A process for preparing a compound according to claim 1 or 2, comprising the steps of converting a ketone or aldehyde of formula (2) into a compound of formula (1);



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and thereafter if necessary:

- i) converting a compound of formula (1) into another compound of formula (1);
- ii) removing any protecting groups;
- iii) forming a pharmaceutically acceptable salt or *in vivo* hydrolysable ester